

Application No. 10/018,080
 Amendment of April 7, 2004
 Response to the Notice of Allowability of February 5, 2004

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-50 (Previously Cancelled)

51. (Currently Amended) A method for measuring a concentration of hemoglobin and bilirubin in a sample of blood serum or blood plasma before analysis of said sample by an in vitro diagnostic method, in order to determine whether an amount of hemoglobin, bilirubin or lipid present in that sample can interfere with a measurement of a target analyte contained in said sample by means of said diagnostic method, said method for measuring comprising sequentially carrying out the following method steps:

- (a) carrying out a first method step for determining the concentration of hemoglobin in said sample, said first method step including:
 - i) measuring a first extinction spectrum $E_1(\lambda)$ of said sample in a first selected wavelength range $\lambda_{rh} = \lambda_{1,1}$ to $\lambda_{1,n}$, the contribution of bilirubin to the extinction spectrum being much smaller than the contribution of hemoglobin within the first selected wavelength range, and
 - ii) fitting a first approximated spectrum $\bar{E}_1(\lambda)$ to said first measured extinction spectrum $E_1(\lambda)$, said first approximated spectrum $\bar{E}_1(\lambda)$ being a combination of:
 - a predetermined first approximation function $E_{d1}(\lambda, a_{0h}, a_{1h})$ for a background extinction, with a_{0h}, a_{1h} being coefficients, and
 - a predetermined extinction spectrum $E_H(C_H, \lambda)$ of pure hemoglobin having a concentration C_H to be determined,

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said fitting of said first approximated spectrum $\bar{E}_1(\lambda)$ to said first measured extinction spectrum $E_1(\lambda)$ being performed by varying said concentration C_H of hemoglobin and said coefficients a_{0h} , a_{1h} , so that a deviation between said first measured extinction spectrum $E_1(\lambda)$ and said first approximated spectrum $\bar{E}_1(\lambda)$ is minimized in order to determine the concentration C_H of hemoglobin, and

(b) carrying out a second method step for determining the concentration of bilirubin in said sample, said second method step including:

i) measuring a second extinction spectrum $E_2(\lambda)$ of said sample in a second selected wavelength range $\lambda_{rb} = \lambda_{2,1}$ to $\lambda_{2,n}$,

ii) fitting a second approximated spectrum $\bar{E}_2(\lambda)$ to said second measured extinction spectrum $E_2(\lambda)$, said second approximated spectrum $\bar{E}_2(\lambda)$ being a combination of:

a predetermined second approximation function $E_{d2}(\lambda, a_{0b}, a_{1b})$ for a background extinction, with a_{0b} , a_{1b} being coefficients, a predetermined extinction spectrum $E_H(C_H, \lambda)$ of hemoglobin having a concentration C_H determined in said first method step, and

a predetermined extinction spectrum $E_B(C_B, \lambda)$ of pure bilirubin having a concentration C_B to be determined,

said fitting of said second approximated spectrum $\bar{E}_{1+2}(\lambda)$ to said second measured extinction spectrum $E_{1+2}(\lambda)$ being performed by varying said concentration C_B of bilirubin and said coefficients a_{0b} , a_{1b} , so that a deviation between said second measured extinction spectrum $E_2(\lambda)$ and said second approximated spectrum $\bar{E}_2(\lambda)$ is minimized in order to determine the concentration C_B of bilirubin.

52. (Previously presented) The method of claim 51 wherein:

said first approximated spectrum $\bar{E}_1(\lambda)$ is the sum of said predetermined first approximation function $E_{d1}(\lambda, a_{0h}, a_{1h})$ for the background

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extinction, and said predetermined extinction spectrum $E_H(C_H, \lambda)$ of hemoglobin having a concentration C_H , to be determined; and

said second approximated spectrum $\hat{E}_2(\lambda)$ is the sum of said predetermined second approximation function $E_{d2}(\lambda, a_{0b}, a_{1b})$ for the background extinction, said predetermined extinction spectrum $E_H(C_H, \lambda)$ of hemoglobin having a concentration C_H and said predetermined extinction spectrum $E_B(C_B, \lambda)$ of bilirubin having a concentration C_B to be determined.

53. (Previously presented) The method of claim 51 wherein in order to determine whether the amount of lipid present in said sample can interfere with the measurement of the target analyte contained in said sample by means of said diagnostic method, said measuring method further comprises carrying a third method step for obtaining a differential spectrum $E_{diff}(\lambda)$ which is representative of the amount of lipid contained in said sample, said differential spectrum being defined by

$$E_{diff}(\lambda) = E(\lambda) - E_H(\lambda) - E_B(\lambda)$$

wherein $E(\lambda)$ comprises said first measured extinction spectrum $E_1(\lambda)$ and said second measured extinction spectrum $E_2(\lambda)$,

wherein $E_H(\lambda)$ is the contribution of hemoglobin to the spectrum said contribution being obtained by said first method step, and

wherein $E_B(\lambda)$ is the contribution of bilirubin to the spectrum said contribution being obtained by said second method step.

54. (Previously presented) The method of claim 51 wherein said fitting of said approximated spectra to said measured values of extinction spectra is done by a last squares fitting method.

55. (Previously presented) The method of claim 51 wherein said sample is marked as anomalous if the concentration of hemoglobin or the concentration of bilirubin or both are outside of a predetermined range.

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56. (Previously presented) The method of claim 53 wherein said differential spectrum $E_{\text{diff}}(\lambda)$ is computed over a wavelength range covering at least 30 % of the whole wavelength range defined by the broadest combination of said first wavelength range defined by $\lambda_{1,1}$ and $\lambda_{1,n}$, and said second wavelength range defined by $\lambda_{2,1}$ and $\lambda_{2,n}$, and the differential spectrum is subjected to an analysis in view of anomalies.

57. (Previously presented) The method of claim 53 wherein said differential spectrum $E_{\text{diff}}(\lambda)$ is computed over a wavelength range covering at least 50 % of the whole wavelength range defined by the broadest combination of said first wavelength range defined by $\lambda_{1,1}$ and $\lambda_{1,n}$, and said second wavelength range defined by $\lambda_{2,1}$ and $\lambda_{2,n}$.

58. (Previously presented) The method of claim 53 wherein said differential spectrum $E_{\text{diff}}(\lambda)$ is computed over a wavelength range covering about 100 % or more of the whole wavelength range defined by the broadest combination of said first wavelength range defined by $\lambda_{1,1}$ and $\lambda_{1,n}$, and said second wavelength range defined by $\lambda_{2,1}$ and $\lambda_{2,n}$.

59. (Previously presented) The method of claim 56 wherein the curvature or the slope of the differential spectrum $E_{\text{diff}}(\lambda)$ in at least one predetermined wavelength range is determined, the result compared with the expected value, and wherein the differential spectrum is estimated to be normal if the value compared have identical sign.

60. (Previously presented) The method of claim 56 wherein the curvature and the slope of the differential spectrum $E_{\text{diff}}(\lambda)$ in at least one predetermined wavelength range is determined, the results compared with the

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expected values, and wherein the differential spectrum is estimated to be normal if the values compared have identical sign.

61. (Previously presented) The method of claim 56 wherein the curvature or the slope of the differential spectrum $E_{\text{diff}}(\lambda)$ in at least one predetermined wavelength range is determined, the result compared with the expected value, and wherein the differential spectrum is estimated to be normal if the value compared have identical sign, with the magnitude resting in a predetermined range given by an upper and a lower limiting curve.

62. (Previously presented) The method of claim 56 wherein the curvature and the slope of the differential spectrum $E_{\text{diff}}(\lambda)$ in at least one predetermined wavelength range is determined, the results compared with the expected values, and wherein the differential spectrum is estimated to be normal if the values compared have identical sign, with the magnitude resting in a predetermined range given by an upper and a lower limiting curve.

63. (Previously presented) The method of claim 51 wherein the first wavelength range is chosen in the range of about 500 to about 600 nanometer, and the second wavelength range is chosen in the range of about 400 to about 600 nanometer.

64. (Previously presented) The method of claim 51 wherein the first wavelength range is chosen in the range of about 545 to about 575 nanometer, and the second wavelength range is chosen in the range of about 480 to about 545 nanometer.

65. (Previously presented) The method of claim 51 wherein the first wavelength range is from about 545 to about 575 nanometer, and the second wavelength range is from about 480 to about 545 nanometer.

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66. (Previously presented) The method of claim 63 wherein said sample is estimated to be of critical condition if the concentration of hemoglobin or the concentration of bilirubin or both are outside of a predetermined range.

67. (Previously presented) The method of claim 53 wherein the first wavelength range is chosen in the range of about 500 to about 600 nanometer, and the second wavelength range is chosen in the range of about 400 to about 600 nanometer.

68. (Previously presented) The method of claim 53 wherein the first wavelength range is chosen in the range of about 545 to about 575 nanometer, and the second wavelength range is chosen in the range of about 480 to about 545 nanometer.

69. (Previously presented) The method of claim 53 wherein the first wavelength range is from about 545 to about 575 nanometer, and the second wavelength range is from about 480 to about 545 nanometer.

70. (Previously presented) The method of claim 67 wherein said sample is estimated to be of critical condition if the differential spectrum is anomalous.

71. (Previously presented) The method of claim 67 wherein the amount of lipid and the overall constitution of the sample are estimated to be normal if the differential spectrum has a negative slope or a positive curvature or both.

72. (Previously presented) The method of claim 51, wherein the spectra are provided as electrical signals and furnished to an evaluation device

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comprising a processor which performs the method steps on the spectra under the control of a program, and wherein the results are stored in a storage means or presented to an operator.

73. (Previously presented) The method of claim 53, wherein the spectra are provided as electrical signals and furnished to an evaluation device comprising a processor which performs the method steps on the spectra under the control of a program, and wherein the results are stored in a storage means or presented to an operator.

74. (Previously presented) The method of claim 72, wherein the storage means is a storage means for digital data.

75. (Previously presented) The method of claim 73, wherein the storage means is a storage means for digital data.

76. (Previously presented) The method of claim 74, wherein the data are presented to an operator by printing, displaying or audible sounds.

77. (Previously presented) The method of claim 75, wherein the data are presented to an operator by printing, displaying or audible sounds.